

Patients' inability to perform a preoperative cardiopulmonary exercise test or demonstrate an anaerobic threshold is associated with inferior outcomes after major colorectal surgery

C. W. Lai^{1,2}, G. Minto^{2,3}, C. P. Challand^{1,2}, K. B. Hosie¹, J. R. Sneyd^{2,3}, S. Creanor² and R. A. Struthers^{2,3*}

¹ Department of Colorectal Surgery, Derriford Hospital, Plymouth, UK

² Plymouth University Peninsula Schools of Medicine and Dentistry, Plymouth, UK

³ Department of Anaesthesia, Derriford Hospital, Plymouth, UK

* Corresponding author: Department of Anaesthetic, Plymouth Hospitals NHS Trust, Derriford Hospital, Derriford Road, Derriford, Plymouth PL6 8DH, UK. E-mail: richardstruthers@nhs.net

Editor's key points

- Cardiopulmonary exercise testing (CPET) tests the ability of the cardio-respiratory systems to deliver oxygen to tissues under stress and provides an objective measure of functional capacity and impairment.
- A lower anaerobic threshold indicates lower aerobic fitness.
- Consistent with previous studies, these investigators have shown that poor performance on CPET is associated with inferior postoperative outcomes.
- More importantly, there seems to be a small proportion of patients who are unable to complete CPET and these have the longest hospital stay and poorest survival.

Background. Surgical patients with poor functional capacity, determined by oxygen consumption at anaerobic threshold (AT) during cardiopulmonary exercise testing (CPET), experience longer hospital stays and worse short- and medium-term survival. However, previous studies excluded patients who were unable to perform a CPET or who failed to demonstrate an AT. We hypothesized that such patients are at risk of inferior outcomes after elective surgery.

Methods. All patients undergoing major colorectal surgery attempted CPET to assist in the planning of care. Patients were stratified by their test results into Fit ($AT \geq 11.0 \text{ ml O}_2 \text{ kg}^{-1} \text{ min}^{-1}$), Unfit ($AT < 11.0 \text{ ml O}_2 \text{ kg}^{-1} \text{ min}^{-1}$), or Unable to CPET groups (failed to pedal or demonstrate an AT). For each group, we determined hospital stay and mortality.

Results. Between March 2009 and April 2010, 269 consecutive patients were screened, and proceeded to bowel resection. Median hospital stay was 8 days (IQR 5.1–13.4) and there were 44 deaths (16%) at 2 yr; 26 (9.7%) patients were categorized as Unable to CPET, 69 (25.7%) Unfit and 174 (64.7%) Fit. There were statistically significant differences between the three groups in hospital stay [median (IQR) 14.0 (10.5–23.8) vs 9.9 (5.5–15) vs 7.1 (4.9–10.8) days, $P < 0.01$] and mortality at 2 yr [11/26 (42%) vs 14/69 (20%) vs 19/174 (11%), respectively ($P < 0.01$)] although the differences between Unable and Unfit were not statistically different.

Conclusions. Patients' inability to perform CPET is associated with inferior outcomes after major colorectal surgery. Future studies evaluating CPET in risk assessment for major surgery should report outcomes for this subgroup.

Keywords: exercise test; general surgery; length of stay; mortality; preoperative care; risk assessment

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In the UK, elective surgical procedures have an overall in-hospital mortality of 0.4%. However, the figures conceal that a large proportion of the mortality is concentrated in a group of high-risk patients undergoing major surgery.¹

Recent prominent reports have highlighted deficiencies in the identification of the high-risk surgical patient and appropriate planning of their perioperative care. Patients may be undergoing major procedures without having a full appreciation of the risk of mortality and severe complications that they face.^{2,3}

The Royal College of Surgeons' report, 'Peri-operative Care of the Higher Risk General Surgical Patient', recommends the use of scoring systems to estimate patients' risk of mortality and guide escalation of care for those with an expected mortality >5%.³

Major surgery triggers a strong systemic inflammatory response, which leads to an increase in oxygen demand. This is met by an increase in global oxygen delivery (DO_2), through an increase in cardiac output (CO) and increase in tissue oxygen extraction. While most patients are able to mount an

adequate response, there is a group who may not have the required physiological reserve. This group is at a higher risk of morbidity and mortality when undergoing major surgery.^{4,5}

Cardiopulmonary exercise testing (CPET) examines the ability of the cardio-respiratory system to deliver oxygen to tissues under stress and provides an objective determination of functional capacity and impairment. Anaerobic threshold (AT) is the point during exercise when anaerobic metabolism supplements aerobic with additional CO₂ production, creating an inflection point on a plot of pulmonary CO₂ efflux vs O₂ uptake. Lower AT indicates lower aerobic fitness and is associated with increased postoperative mortality and severe morbidity. However, CPET studies to date have not reported the perioperative outcomes of those unable to perform a test or in whom an AT was not determined.^{6–11} Patients with heart failure who do not demonstrate an AT are at higher risk of major cardiac events. This may be attributable to a short duration of tests or abnormal ventilatory patterns which attenuate the inflection point or alterations in cardiovascular physiology, which conceal AT in the early part of the test.¹² We hypothesized that patients undergoing surgery who do not demonstrate an AT may similarly be at high risk of adverse outcomes.

Methods

All patients undergoing elective major colorectal surgery at our Colorectal Specialist Unit attempt preoperative CPET to assist in the planning of perioperative care. With Ethics Committee approval all patients undergoing bowel resection between March 2009 and April 2010 were screened for inclusion into a trial of intraoperative goal-directed fluid therapy and those with an AT > 8 ml O₂ kg⁻¹ min⁻¹ were approached to be enrolled and randomized. The testing methods and results of this study have been previously reported.¹¹ CPET was performed on a stationary bicycle (Zan, nSpire, CO, USA) using a ramped exercise protocol with AT determined by V slope and ventilatory equivalents.

All patients tested during this period were asked for permission to audit their outcomes. Patients were stratified by their CPET results into Fit (AT ≥ 11.0 ml O₂ kg⁻¹ min⁻¹), Unfit (AT < 11.0 ml O₂ kg⁻¹ min⁻¹), or Unable to CPET if they failed to pedal the cycle or demonstrate an AT.

Patient characteristics and 'end of surgery' colorectal POSSUM (CR-POSSUM) predicted percentage mortality were recorded, along with type of surgery (laparoscopic or open), use of critical care, length of hospital stay, and 30-day-, 90-day- and 2-yr mortality. All patients were cared for on our Specialist Colorectal surgical unit.

Analysis

Data were collated into Microsoft Excel and statistical analysis performed using MiniTab (Minitab® Statistical software v16, USA). Statistical significance was set at the 5% level. Data are presented as mean [standard deviation (SD)] where normally distributed and median (interquartile range) where not normally distributed. Between fitness group differences in total length of hospital stay were tested using one way analysis of

variance (ANOVA) after log transformation of non-parametric data. Categorical data were compared between fitness groups using χ^2 tests. Where there was evidence of overall differences between the three fitness groups, Bonferroni-corrected follow-up multiple comparisons were used to identify between which pairs of groups had statistically significant differences. A survival plot, stratified by fitness groups, was performed using the Kaplan–Meier method with survival distributions compared using the log-rank test. Multivariable binary logistic regression was also undertaken to examine whether fitness group had a significant influence on the probability of death by 2-yr post-surgery, after allowing for other important variables (age, gender, and Dukes staging of malignancy).

Results

Between March 2009 and April 2010, 287 patients attended clinic and attempted CPET; 269 proceeded to surgery with follow-up, five formally declined to be followed up, and 13 did not proceed to surgery. One hundred and seventy-nine patients were recruited to the trial of intraoperative fluid management.¹¹ All consenting survivors were followed to 2 yr. A summary of the results, stratified by CPET fitness group, is presented in Table 1.

Thirteen patients did not proceed to bowel resection—five who would have been characterized as Fit, five Unfit and three as Unable to CPET. A summary of their results and reasons for not proceeding are presented as a web-based Supplementary Table S1.

For the cohort proceeding to surgery median hospital stay was 8 days (IQR 5.1–13.4) and there were 44 deaths at 2 yr (16%).

Twenty-six (9.7%) patients were categorized as Unable to CPET, 69 (25.7%) Unfit and 174 (64.7%) as Fit. Of the Unable patients 15 had a measured VO₂ peak but there was no AT demonstrable on V slope or ventilatory equivalents. The other 11 did not produce a test—seven because of arthritis, three because of frailty and one because of perineal pain.

The Unable patients were, on average, older than Unfit and Fit patients and typically had higher CR-POSSUM percentage predicted mortality although there was insufficient evidence to support a statistically significant difference between Fit and Unfit groups. The Unable group had higher mortality at each time point, and in particular at 2 yr [11/26 (42%) vs 14/69 (20%) vs 19/174 (11%), $P < 0.01$], although again there was insufficient evidence to support a statistically significant difference between the Unfit and Unable groups.

Kaplan–Meier survival curves are presented in Figure 1; there was evidence of significant differences in the survival distributions of the three groups ($P < 0.01$).

Binary logistic regression analysis was performed looking at main effects on probability of death at 2 yr after surgery. Results are presented in Table 2. Age at surgery was associated with an odds ratio of 1.09 per year [95% confidence interval (CI) 1.04–1.14] and CR-POSSUM Score at the end of surgery with an odds ratio of 1.17 (1.08–1.28) per percentage increase in predicted mortality. Male gender and Dukes C or D cancer staging (compared with non-malignant disease) were also

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